

## REMARKS

Applicants have amended claim 1 to expedite prosecution. Support for this amendment can be found throughout the specification, and particularly, Figure 2 and the accompanying text, at page 25, last paragraph, and at page 26, lines 6-8, and second full paragraph. Accordingly, the amendment is supported by the specification as filed and does not introduce new matter, and its entry is respectfully requested.

Claims 1, 5-7 were rejected under 35 U.S.C. 112, first paragraph, as allegedly containing new matter.

Applicants disagree and submit that the rejection be withdrawn for the following reasons.

Figure 2 shows a construct that produces a fusion protein with a single amino and single carboxyl end, i.e., no stop codon after the antibody encoding sequence and before the protamine encoding sequence. Further, this is explicitly described at p. 25, last paragraph, where the specification states that the Fab105 encoding sequence does not have a stop codon, when it is used in the fusion protein before the nucleic acid binding protein encoding sequence (see also p. 26, line 6-8, and second full par.). The meaning of this is that the fusion protein has only a single amino and a single carboxyl end.

Accordingly, to make explicit that which was implicit, and to expedite prosecution, Applicants have amended claim 1, to specifically point out there is no stop codon between the antibody encoding sequence and the nucleic acid binding protein encoding sequence.

In light of the above, Applicants respectfully submit that the claims 1, and 5-7 comply with 35 U.S.C. 112, first paragraph, and that the rejection should be withdrawn.

Claims 1, 3-5, and 5-17 were rejected as being unpatentable under 35 U.S.C. 103 over Beug et al., Chaudhary et al. and Wu et al.

Applicants disagree and submit that the rejection be withdrawn for the following reasons.

The Examiner contends that the specification as written does not mention the efficacy and superior performance of the claimed system over other systems, such as Wu.

This is simply not true. For example, page 23, second full paragraph teaches that the construct of the present invention provides a superior delivery method compared to prior art. Specifically, one that can be efficiently produced and provide high binding activity. Further, the last paragraph of page 38 continuing into and through page 39, specifically discusses the reasons why this method provides a more efficient delivery system as compared to prior art, such as Wu. For example, when discussing the

advantages of the present system for delivering immunotoxins to the cells, the specification reads “[f]urthermore, the bifunctional recombinant fusion proteins as a gene carrier also have the advantage over chemically linked ones [citing references including Wu], such as **efficient production**, and potentially **better binding activity**” (page 39). Neither Chaudhary nor Beug provide any evidence why delivery of nucleic acids using a fusion protein of the present invention would be superior to Wu, whereas the present application clearly describes the benefits provided by this system over, e.g. Wu. Accordingly, contrary to what the Examiner argues, the Applicants clearly taught and described the advantages of this system in the specification. The Declaration and additional data confirm this teaching.

Although the Examiner contends that use of a targeting antibody would be generally expected to provide a more selective targeting, those working in the art at that time show this statement is wrong. Both Wu and Beug were looking at **targeting receptors**. **They chose to use a ligand instead of an antibody**.

As discussed before in the record, none of the references cited by the Examiner discuss the significant benefits provided by the claimed antibody targeted delivery system. Without having read the disclosure of the Applicants, i.e. without the benefit of unpermitted hindsight, a skilled artisan would not have been motivated to use a recombinant fusion protein technology such as that described by Beug with a targeting moiety comprising an **antibody** or an antigen targeting fragment thereof to deliver nucleic acids to cells.

Moreover, Applicants respectfully submit that none of the cited references teach delivery of RNA, as claimed in claim 17. As pointed out by Rossi et al., Nature Biotechnology 23:682-684 (2005) delivering RNA is difficult. The present construct successfully delivers RNA, such as siRNA, as taught. Therefore, in addition to not teaching an antibody fusion protein, even all the elements of claim 17 are not present in the cited prior art, and thus the rejection over 103 is not appropriate. Accordingly, Applicants submit that claim 17 is in condition for allowance.

In light of the above, Applicants respectfully submit that this rejection should be withdrawn.

Claim 6 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Beug et al. in view of Chaudhary et al. and Wu et al as applied to Claims 1, 3 – 5, and 7 – 16, and further in view of Ryder et al.

Applicants submit that this rejection should be withdrawn for the following reasons.

Applicants respectfully submit that the addition of Ryder et al. to the combination in no way overcomes the essential deficiency of the references discussed above. Ryder in no way discloses using such nucleic acid binding domain to deliver nucleic acids to cells as part of a fusion protein, nor provides

any motivation to the skilled artisan to consider such system. Neither thus Ryder talk about the specific benefits of delivering nucleic acids using antibody as a targeting moiety. Thus, Ryder cannot cure the fundamental defect in the original combination of references, which do not teach the use of an **antibody fusion protein** for selective delivery of a nucleic acids.

The Examiner did not reject or object to claim 17. Applicants agree, and submit that claim 17 is in condition of allowance. None of the cited prior art references use any of the described delivery methods in delivery of RNA. Therefore, in addition to not teaching an antibody fusion protein, even all the elements of claim 17 are not present in the cited prior art, and thus the rejection over 103 is not appropriate.

Accordingly, Applicants submit that claim 17 is in condition for allowance as is.

Accordingly, for the reasons of record which are repeated herein, and for the reasons mentioned above, this rejection of the claims should also be withdrawn.

Accordingly, Beug et al., Chaudhary et al. and Wu et al. or Ryder et al. teach nothing whatsoever of the claimed method. Thus, the rejection should be withdrawn.

In view of the foregoing arguments and amended claims, Applicants respectfully submit that claims 1, 3-17 comply with both 35 U.S.C. §103(a) and §112, first paragraph.

In view of the foregoing, applicants respectfully submit all claims are in condition for allowance. Early and favourable action is requested.

Respectfully submitted,

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